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EDITORIAL

Mucosal Diseases series

The oral mucous membrane has features similar to skin but also differs in several ways. This series of seven reviews by internationally acknowledged expert stomatologists and dermatologists, reviews the aspects of epithelial biology and aetiopathogenesis necessary for the diagnosis of the vesiculoerosive disorders, and updates management.

This is a heterogeneous group of disorders. The most serious, pemphigus, is a group of potentially life-threatening autoimmune diseases characterized by cutaneous and/or mucosal blistering. Pemphigus vulgaris, the most common variant, is characterized by circulating antibodies directed against desmoglein 3. There is a fairly strong genetic background with linkage to HLA class II alleles and ethnic groups such as Ashkenazi Jews and those of Mediterranean and Indian origin, are especially liable. Biopsy of perilesional tissue, with histological and immunostaining examination are essential to the diagnosis. Serum autoantibodies are best detected using both normal human skin and monkey oesophagus or by enzyme-linked immunosorbent assay. Current treatment is largely based on systemic immunosuppression using corticosteroids, with azathioprine or other adjuvants or alternatives but newer therapies with potentially fewer adverse effects, also appear promising.

Mucous membrane pemphigoid (MMP) is a fascinating sub-epithelial vesiculobullous disorder but it is now quite evident that a number of disorders may produce similar clinical pictures. Furthermore, a range of variants of MMP exist, with antibodies directed against various hemidesmosomal components or components of the epithelial basement membrane. The term immune-mediated sub-epithelial blistering diseases (IMSEBD) has therefore been used. Immunological differences may account for the significant differences in their clinical presentation and responses to therapy but unfortunately data on this are few. The diagnosis and management of IMSEBD on clinical grounds alone is impossible. Biopsy with immunostaining is now invariably required, sometimes supplemented with other investigations. No single treatment regimen reliably controls all these disorders, and it is not known if the specific subsets of MMP will respond to different drugs. Currently, apart from improving oral hygiene, immunomodulatory, especially immunosuppressive, therapy is typically used to control oral lesions.

Erythema multiforme (EM) is an acute mucocutaneous hypersensitivity reaction characterized by a skin eruption, with or without oral or other mucous membrane lesions. EM has been classified into a number of different variants based on the degree of mucosal involvement and the nature and distribution of the skin lesions. Stevens–Johnson syndrome (SJS), is where there is extensive skin involvement and significant morbidity and mortality. EM can be triggered by a number of factors, especially preceding infection with herpes simplex virus (HSV), the lesions resulting from a cell-mediated immune reaction triggered by HSV-DNA. SJS is usually initiated by drugs, and the tissue damage is mediated by soluble factors including Fas and FasL.

Oral lichen planus is a common chronic inflammatory disorder affecting stratified squamous epithelia, probably a T-cell-mediated autoimmune disease in which auto-cytotoxic CD8+ T cells trigger apoptosis of oral epithelial cells.

An oral biopsy with histopathologic study is recommended to confirm the clinical diagnosis and mainly to exclude dysplasia and malignancy. The most commonly employed and useful agents for the treatment of LP are topical corticosteroids but other newer agents are available.

Recurrent aphthous stomatitis (RAS; aphthae; canker sores) is a common condition, the aetiology of which is not entirely clear. A genetic predisposition is shown by strong associations with genotypes of IL-1β; IL-6, and a positive family history in some patients. Behçet's syndrome (BS; Adamantiades syndrome) is a systemic disorder, in which RAS are associated with genital ulceration, and iridocyclitis. BS has an association with HLA-B5 and HLA-B51 (B5101).

The immunopathogenesis of RAS probably involves a cell-mediated immune response mechanism, and involves generation of T-cells and tumour necrosis factor alpha (TNF alpha) production by these and other leukocytes (macrophages and mast cells). TNF, a major inflammatory mediator, induces initiation of the inflammatory process by its effect on endothelial cells adhesion and a chemotactic effect on neutrophils. Elevated levels of interleukin-2 (IL-2) (another pro-inflammatory cytokines) and lower levels of IL-10 (an anti-inflammatory cytokine) have been found. Natural killer cells activated by IL-2 play a role in the process of this disease. Topical corticosteroids can often control RAS. In BS, features such as arthralgia and leucocytoclastic vasculitis suggest an immune-complex mediated basis, which is supported by finding circulating immune complexes and, although the antigen responsible is unidentified, heat shock proteins have been implicated. Topical corticosteroids can help in BS but, apart from improving oral hygiene, immunomodulatory, especially immunosuppressive, therapy is typically used to control oral lesions.

Correspondence: Crispian Scully, Eastman Dental Institute, University College London, 256 Grays Inn Road, London WC1X 8LD, UK.
Tel: +44 (0) 20 7915 1038, Fax: +44 (0) 20 7915 1039,
E-mail: c.scully@eastman.ucl.ac.uk